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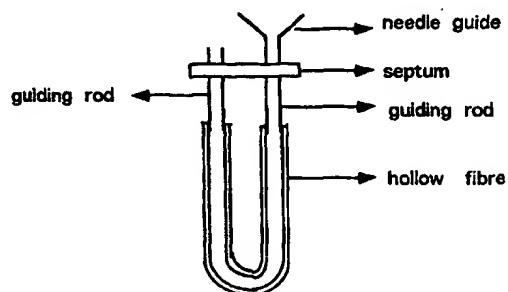
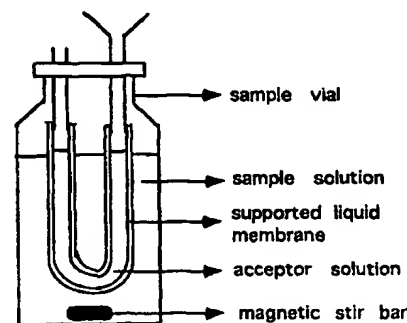
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : G01N 1/40	A1	(11) International Publication Number: WO 00/33050 (43) International Publication Date: 8 June 2000 (08.06.00)
(21) International Application Number: PCT/NO99/00359 (22) International Filing Date: 30 November 1999 (30.11.99) (30) Priority Data: 19985613 1 December 1998 (01.12.98) NO (71)(72) Applicants and Inventors: RASMUSSEN, Knut, E. [NO/NO]; Gulhellaveien 1, N-1370 Asker (NO). KROGH, Mette [NO/NO]; Maridalsveien 235B, N-0467 Oslo (NO). PEDERSEN-BJERGAARD, Stig [NO/NO]; Sollidgrenda 82, N-0491 Oslo (NO). (74) Agent: HELGERUD, Jan, E.; Bryns Patentkontor A/S, P.O. Box 765, Sentrum, N-0106 Oslo (NO).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: METHOD AND DISPOSABLE DEVICES FOR MICRO EXTRACTION**(57) Abstract**

An apparatus for carrying out liquid-liquid micro extraction or liquid-liquid-liquid micro extraction with high enrichment comprises: a) a container for a sample solution having volume V_s with dissolved substance, analyte, to be analysed, b) a second container arranged in the first container, preferably a disposable container, having permeable membrane walls, for an acceptor solution, having volume V_a , wherein 1) $V_s:V_a \geq 50$ and 2) about $1 \mu\text{l} \leq V_a \leq 50 \mu\text{l}$, c) stirring means, preferably a magnetic bar. The method is applicable for liquid-liquid micro extraction (LLME) and liquid-liquid-liquid micro extraction (LLLME) with high enrichment. In the latter case, a liquid immiscible with the sample solution and the acceptor solution is immobilised in the wall of the container for the acceptor solution. There is also described a disposable device for use in liquid-liquid micro extraction in the form of a sponge body having defined pore volume for absorption of an immobilised acceptor solution for an analyte from a volume of a sample solution.

A**B**

Disposable device for LLMBE (a) and disposable device connected to an autosampler vial (b)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/NO 99/00359

A. CLASSIFICATION OF SUBJECT MATTER IPC7: G01N 1/40 According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC7: G01N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SE,DK,FI,NO classes as above Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	WO 9725606 A1 (RASMUSSEN, KNUT, E.), 17 July 1997 (17.07.97), page 4, line 8 - line 26; page 6, line 9 - line 32 --	1-11		
A	DE 19525771 A1 (HEWLETT-PACKARD CO.), 28 March 1996 (28.03.96), column 2, line 22 - column 3, line 28 --	1-11		
A	WO 9115745 A1 (PAWLISZYN, JANUSZ, B.), 17 October 1991 (17.10.91), page 2, line 28 - page 3, line 19 -- -----	1-11		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; border: none;"> * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td style="width: 50%; vertical-align: top; border: none;"> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family </td> </tr> </table>			* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
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Date of the actual completion of the international search 9 March 2000		Date of mailing of the international search report 14 -03- 2000		
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86		Authorized officer Ulla Granlund/MP Telephone No. +46 8 782 25 00		

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.

PCT/NO 99/00359

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9725606 A1	17/07/97	AU 1457697 A CA 2242481 A EP 0938654 A NO 302056 B NO 960133 A	01/08/97 17/07/97 01/09/99 12/01/98 14/07/97
DE 19525771 A1	28/03/96	JP 8094597 A US 5565622 A	12/04/96 15/10/96
WO 9115745 A1	17/10/91	AT 108018 T AU 654948 B AU 7574191 A CA 2079337 A DE 69102700 D,T DK 523092 T EP 0523092 A,B SE 0523092 T3 ES 2056644 T NO 923826 A US 5691206 A	15/07/94 01/12/94 30/10/91 03/10/91 12/01/95 14/11/94 20/01/93 01/10/94 01/10/92 25/11/97

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

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United States Patent and Trademark
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in its capacity as elected Office

Date of mailing (day/month/year) 25 July 2000 (25.07.00)	
International application No. PCT/NO99/00359	Applicant's or agent's file reference E10928 JH/JB
International filing date (day/month/year) 30 November 1999 (30.11.99)	Priority date (day/month/year) 01 December 1998 (01.12.98)
Applicant RASMUSSEN, Knut, E. et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

16 June 2000 (16.06.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Manu Berrod

Telephone No.: (41-22) 338.83.38

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ART 34 AMST

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 05 APR 2001

WIPO

Applicant's or agent's file reference	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/NO99/00359	International filing date (day/month/year) 30.11.1999	Priority date (day/month/year) 01.12.1998
International Patent Classification (IPC) or national classification and IPC7 G01N 1/40		
Applicant RASMUSSEN, Knut E. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 16.06.2000	Date of completion of this report 27.03.2001
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 08-667 72 88	Authorized officer Ulla Granlund/MP Telephone No. 08-782 25 00

Form PCT/IPEA/409 (cover sheet) (January 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NO99/00359

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed☒ the description:pages 1-13, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☒ the claims:pages 15, 16, as originally filed

pages _____, as amended (together with any statement) under article 19

pages _____, filed with the demand

pages 14, filed with the letter of 05.03.2001☒ the drawings:pages 1-6, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☐ The amendments have resulted in the cancellation of:☐ the description, pages _____☐ the claims, Nos. _____☐ the drawings, sheet/fig _____5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2 (c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NO99/00359

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>1-11</u>	YES
	Claims		NO
Inventive step (IS)	Claims	<u>1-11</u>	YES
	Claims		NO
Industrial applicability (IA)	Claims	<u>1-11</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The claimed invention relates to an apparatus and a method for liquid-liquid or liquid-liquid-liquid micro extraction. It also relates to a disposable device for use in liquid-liquid micro extraction. The invention is intended to solve problems regarding sample pre-treatment involving concentration of analytes to a concentration suitable for detection.

WO 9725666 (page 2 line 28 - page 3 line 19), which represents the closest prior art, discloses a method for liquid-liquid micro extraction. A solvent is immobilized on the surface of a carrier.

However, the cited document does not reveal an apparatus comprising a first container for a sample solution having volume V_s and a second container for an acceptor solution arranged in the first container. The second container has permeable membrane walls and a volume V_A , wherein $V_s: V_A \geq 50$. The sample solution with analyte is stirred until extraction equilibrium is established. The disposable device has the form of a sponge for absorption of acceptor solution.

Therefore, the claimed invention as stated in claims 1-11 is novel. It is further considered to involve an inventive step because of high enrichment of analyte in the acceptor solution. It is also considered to be industrially applicable.

P a t e n t C l a i m s

1.

Apparatus for carrying out liquid-liquid micro extraction or liquid-liquid-liquid micro extraction with high enrichment, c h a r a c t e r i s e d i n that it comprises

- a) a container for a sample solution having volume V_s with dissolved substance, analyte, to be analysed,
- b) a second container arranged in the first container, preferably a disposable container, having permeable membrane walls, for an acceptor solution, having volume V_a , wherein
 - 1) $V_s:V_a \geq 50$ and
 - 2) about $1 \mu\text{l} \leq V_a \leq 50 \mu\text{l}$,
- c) stirring means, preferably a magnetic bar.

2.

Apparatus according to 1, c h a r a c t e r i s e d i n that the container for the acceptor solution is a microporous hollow fibre.

3.

A method according to claims 1 and 2, c h a r a c t e r i s e d i n that the container is a hollow fibre of an active polymer.

4.

A method for liquid-liquid micro extraction with high enrichment by the use of the apparatus according to claim 1, c h a r a c t e r i s e d i n that

- a) the container for acceptor solution is lowered into an acceptor solution so that the membrane wall is impregnated with and the container is filled with a defined volume of the acceptor solution,
- b) the container filled under a) is transferred to the container having a defined volume of the sample solution with the analyte that is sought,
- c) the sample solution with analyte is stirred until extraction equilibrium is established for the analyte in the two solutions, and
- d) the acceptor solution containing enriched analyte is removed from its container for analysis of the analyte.